# Cerebellar-dependent motor learning is based on pruning a Purkinje cell population response

**Nicolas Catz, Peter W. Dicke, and Peter Thier†**

Department of Cognitive Neurology, Hertie Institute for Clinical Brain Research, University of Tübingen, Hoppe-Seyler Strasse 3, 72076 Tübingen, Germany

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**The improvement of motor behavior, based on experience, is a form of learning that is critically dependent on the cerebellum. A well studied example of cerebellar motor learning is short-term saccadic adaptation (STSA). In STSA, information on saccadic errors is used to improve future saccades. The information optimizing saccade metrics is conveyed by Purkinje cells simple spikes (PC-SS) because they are the critical input to the premotor circuits for saccades. We recorded PC-SS of monkeys undergoing STSA to reveal the code used for improving behavior. We found that the discharge of individual PC-SS was unable to account for the behavioral changes. The PC-SS population burst (PB), however, exhibited changes that closely paralleled the qualitatively different changes of saccade kinematics associated with gain-increase and gain-decrease STSA, respectively. Gain-increase STSA, characterized by an increase in saccade duration, replicates the relationship between saccade duration and the end of the PB valid for unadapted saccades. In contrast, gain-decrease STSA, which sports normal saccade duration but reduced saccadic velocity, is characterized by a PB that ends well before the adapted saccade. This suggests that the duration of normal as well as gain-increased saccades is determined by appropriately setting the end of PB end. However, the duration of gain-decreased saccades is apparently not modified by the cerebellum because the PB signals ends too early to determine saccade end. In summary, STSA, and most probably cerebellar-dependent learning in general, is based on optimizing the shape of a PC-SS population response.**

adaptation | cerebellum | primates | saccade | vermis

Improving motor behavior based on learning is a key function of the cerebellum (1–3). What is the code the cerebellum uses to adjust the behavior? To find an answer to this question, we studied short-term saccadic adaptation (STSA), a well known example of cerebellum-dependent motor learning in which information about saccadic errors is used to unconsciously change the metrics of future saccades. In the laboratory, STSA can be demonstrated by shifting the target to be captured by the saccade while the eyes are on their way toward the target (4). This shift is unnoticed because of the absence of accurate visual perception during an ongoing saccade, the so-called saccadic suppression. Because the target is missed by the saccade, a corrective saccade has to be added. As these target shifts are repeated in a consistent manner trial after trial, however, one observes that the metrics of the primary saccade start to change in such a manner as to bring the eyes closer to the final location of the target until after a couple of hundred trials in monkeys, the eyes may reach the target in just one stroke. In other words, a given retinal vector is remapped onto a new saccade vector because it is in any case the target in its initial position that is responsible for the programming of the primary saccade. This remapping depends on the integrity of the oculomotor vermis (OV), comprising lobuli VI and VII, as indicated by the fact that experimental lesions cause an irreversible loss of STSA (5, 6) and related forms of saccadic learning (7). The OV is characterized by a high density of saccade-related Purkinje cells (PCs) (8–10) and low thresholds for microstimulation-evoked saccades (11–14). Many PCs in the OV fire saccade-related simple spike (SS) bursts that collectively encode the duration of normal, unadapted saccadic eye movements (9). Two arguments suggest that the tight correlation between the vermal SS population activity and saccade duration may actually reflect a causal role of the population signal in changing saccade metrics as a consequence of STSA by stopping the saccade at the right point in time. (*i*) Saccade duration and saccade amplitude are tightly correlated. Therefore, stopping an ongoing saccade earlier will lead to a smaller amplitude; conversely, letting it go for a longer time will increase its amplitude. (*ii*) As mentioned before, STSA is permanently abolished by lesions of the OV. Hence, if this deficit were due to a loss of duration control, we would conversely expect that STSA in healthy monkeys should lead to correlated changes of saccade amplitude and the timing of the SS population burst. Here, we report that this is indeed the case for gain-increase adaptation (outward adaptation), i.e., adaptation leading to increases in saccade amplitude. However, because this relationship does not hold for gain-decrase adaptation (inward adaptation), causing a decrease in saccade amplitude, we suggest a refinement of the simple hypothesis that draws on newly discovered behavioral differences between gain-increase and gain-decrease STSA.

## Results

In an attempt to clarify how OV PCs generate STSA, we recorded SS of OV PCs from two rhesus monkeys during two different forms of STSA, termed inward and outward adaptation, respectively. During inward adaptation, the target is shifted back from its original location by a few degrees in the direction of the fovea, prompting a decrease in saccade amplitude. Conversely, during outward adaptation, the shift moves the target farther away from the fovea, causing an increase in saccade amplitude. Of >800 PCs in vermal lobuli VI and VIIA, whose SS could be isolated, 212 (135 in monkey N and 77 in monkey E) could be kept track of during a complete adaptation experiment, consisting of an initial block of visually guided saccades before adaptation and a subsequent block in which adaptation was allowed to develop until a maximal and stable level of gain change (>15%) was established. Individual PCs were randomly assigned to inward adaptation or to outward adaptation. Of the 212 PCs for which complete datasets were available, 128 were studied during outward adaptation, and 84 were studied during inward adaptation.

Fig. 1 depicts the SS as well as the accompanying complex spike (CS) responses of exemplary PCs, three of them recorded during inward adaptation (Fig. 1 *A–C*: PCs 1, 2, 3) and three recorded during outward adaptation (Fig. 1 *D–F*: PC 4,5,6). Four of the PCs (Fig. 1 *A–D*: PCs 1, 2, 3, 4) exhibited saccade-related bursts, strongest in individually varying directions, whereas the fifth one (Fig. 1*E*: PC 5) displayed a weak dip right after saccade onset (PC 5) and the sixth one (Fig. 1*F*: PC 6) displayed a strong saccade-

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†To whom correspondence should be addressed. E-mail: thier@uni-tuebingen.de.

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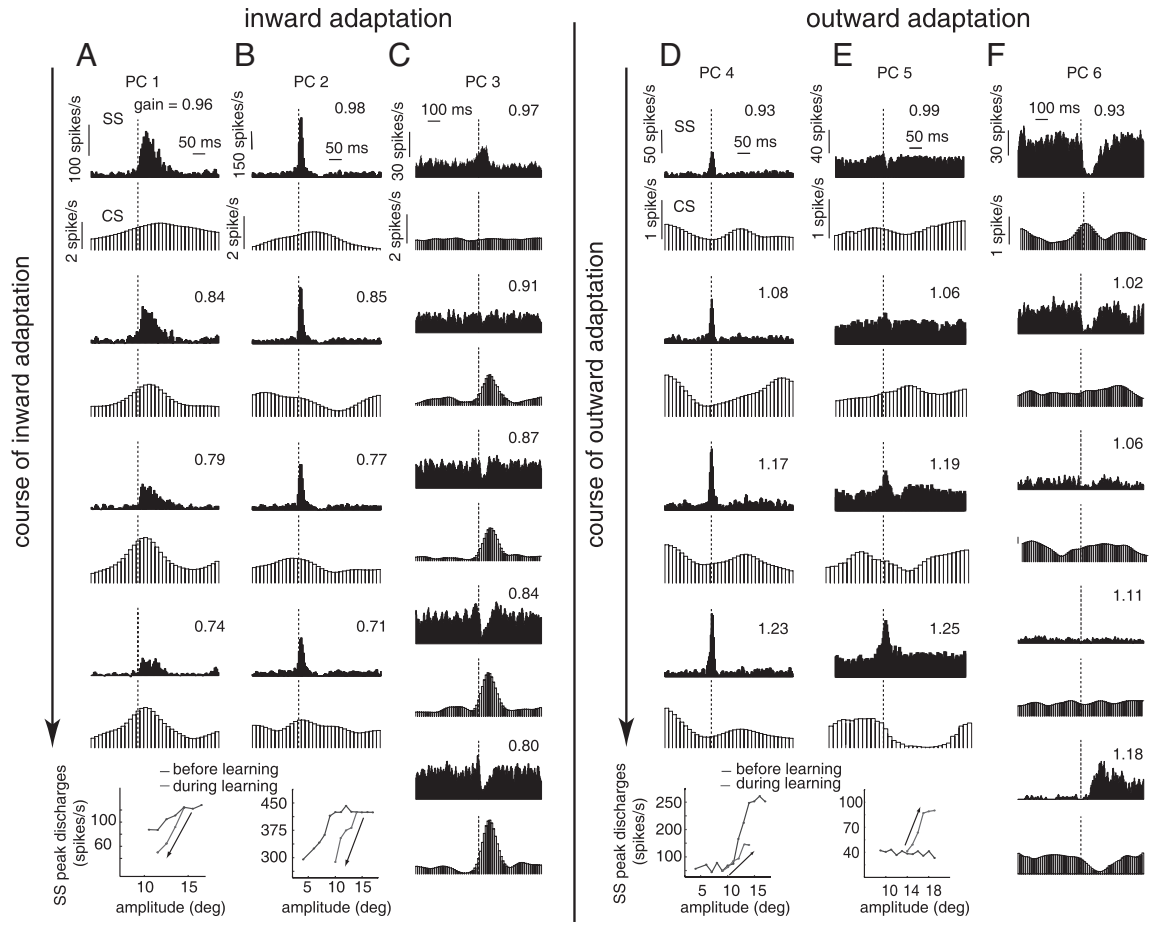


**Fig. 1.** Change in PC responses during STSA. (*A–C*) Three examples of PC-SS and CS responses recorded during inward STSA. (*D–F*) Three examples of PC-SS and CS responses recorded during outward STSA. For each column, the peristimulus histograms (PSTH) represent the mean saccade-related activity of the cell at different times during STSA from the beginning (topmost) to the end (bottommost) of adaptation, each PSTH is based on 50 trials, as a function of the time relative to saccade onset (the vertical dashed line on each PSTH). The number given on top of each PSTH indicates the mean saccadic gain for the group of trials underlying the PSTH. For PCs 1, 2, 4, and 5, the bottommost row depicts the amplitude tuning of a neuron before (blue curve) and during (red curve) adaptation. The arrow indicates the course of adaptation. The CS responses were taken from a recent study on the influence of STSA on CS discharge patterns (20).

related pause. All PCs showed clear changes of their responses during saccadic adaptation. Although the saccade-related bursts of two PCs observed during inward adaptation decreased with decreasing saccade gain resulting from adaptation (PCs 1 and 2), the saccade-related burst of PC 4, observed during outward adaptation, grew over the course of adaptation. Much more profound changes were exhibited by PCs 3, 5, and 6. PC 3 started inward adaptation as a saccade-related burst neuron and ended it as a clear saccade-related pause neuron. In contrast, PC 5 started outward adaptation as an omni-pause neuron and emerged from adaptation as a saccade-related burst neuron. PC 6, which was tested during outward adaptation, showed the most dramatic changes. It started out with a saccade-related pause, interrupting a high frequency background discharge. Although the background activity decreased in the course of adaptation, the saccade-related pause disappeared, and at adaptation offset, a strong postsaccadic response had developed. The simple and complex spike waveforms that underlay the detection of SS and CS events are presented at high temporal resolution in supporting information (SI) Fig. S1 for PCs 1–5 (not available for PC 6). As the waveforms did not change in the course of the experiments, we are confident that the changes of the responses described before were not artifacts of poor isolation of these PCs. The same conclusion can be drawn for PC 6 in view of the consequence of extinction for the firing pattern of PC 6. As shown in Fig. S2, the peculiar changes of the firing pattern observed during adaptation completely reverted during the course of extinction from gain-increase adaptation until—at the end of the extinction period—the original baseline pattern exhibited by this PC before adaptation had commenced was displayed again.

Saccadic adaptation changes saccade amplitude. Hence, the changes in discharge rates during saccadic adaptation exhibited by these exemplary PCs might simply reflect the amplitude dependence of their discharge. However, this is not the case because discharge rates during adaptation never lay on the amplitude tuning curves collected before adaptation (Fig. 1 *A*, *B*, *D*, and *E*, *Lower*). Could the changes observed during adaptation simply reflect an instability of the discharges that become manifest owing to the long time that saccadic adaptation requires in monkeys? This does not seem to be the case, as suggested by observations on a group of 12 PCs with saccade-related bursts, studied when monkeys were asked to make repetitive nonadapted saccades over periods comparable with those needed for adaptation, however, without adaptation taking place. None of these 12 PCs showed significant changes of their response in the absence of adaptation, although a few individual PCs exhibited a subtle and nonsignificant tendency of their peak discharge to be delayed. On the other hand, of the 212 PCs tested during saccadic adaptation, 120 (57%) exhibited significant changes, whereas 43% of these PCs were not influenced by adaptation.

Specifically, during inward adaptation, 54 PCs (64%) of the 84 tested changed, whereas 30 of them showed no change (36%).

Thirty-seven PCs exhibited decreases of saccade-related bursts (44%), with the burst sometimes disappearing completely. Twelve PCs, which did not show any saccade-related responses before adaptation, exhibited a saccade-related pause later (14%), and five (6%) showed idiosyncratic changes (e.g., burst to pause, Fig. 1*A*, PC3). On the other hand, during outward adaptation, 66 PCs (52%) of the 128 tested changed. Of them, 43 PCs (65% of the 66 neurons), which had not shown any saccade-related burst before adaptation, gradually developed such a modulation during adaptation. The discharge of 23 PCs (35% of the 66 neurons) changed in an idiosyncratic manner [pause to burst, pause to postsaccadic responses (e.g., PC 6 in Fig. 1*F*)]. Forty PCs of the whole group showed saccade-related bursts before and after adaptation (31%) without any significant change. The remaining 22 neurons (17%) did not show any saccade-related responses (burst, pause, or postsaccadic activity), either before or after adaptation, or were neurons that showed a saccade-related pause before as well as after adaptation. It seems that saccadic adaptation prompts changes in the discharge patterns of PCs, which can be perplexingly different. However, although the adaptation modifies the discharge patterns, it leaves the level of background activity unaffected (Fig. S3). The inconsistency of the changes of the discharge patterns precludes the deduction of a simple rule on the relationship of discharge changes to adaptation. The absence of such a rule for individual PCs may be less surprising if one recalls the fact that several hundred PCs converge on individual target neurons in the deep cerebellar nuclei (DCN) (15). Hence, we may assume that the DCN target neuron will not be able to discern discharge patterns of individual PCs. In other words, it should be the collective discharge of all PCs, feeding a particular DCN target neuron that matters—largely independently of the specifics of individual contributions. Actually, we were recently able to provide support for the idea that information from PCs is read out in a population format in a study of normal visually guided saccades. In this study, unlike the saccade-related bursts of individual PCs, the calculated collective instantaneous discharge rate (population burst) of larger group of PCs gave a precise description of the timing of saccades (9). With these considerations in mind, we computed population responses for the two groups of PCs studied during inward and outward adaptation, respectively, and scrutinized their behavior during saccadic adaptation (Fig. 2). Population responses were calculated by sorting the responses of individual PCs according to saccade duration (bin width, 2.5 ms). For each saccade duration, we then computed compound perisaccadic histograms with a bin width of 1 ms, smoothed by a Gaussian filter with a standard deviation of 5 ms. Burst onset and offset were defined by a 4 × baseline criterion (9). The preadaptation PB is shown in Fig. 2*A* based on all $n = 212$ PCs (8,226 saccades) and in Fig. S4 separately for the two groups of PCs subjected to inward and outward adaptation, respectively. In both figures, the PB is plotted as it develops over time (*x* axis) for saccades of 45–75 ms durations (*y* axis). In full accordance with our previous report (9), the two figures show that—independently of the composition of the PC groups—the PB starts 50 ms before saccade onset, peaks at saccade onset, and ends at the time the saccade ends, independently of the duration of the saccade. The tight temporal relationship between burst end and saccade end is expressed by the almost perfect linear regression between the two variables (Fig. S5*A*, burst end = 14.8088 ms + 0.7882* saccade end, $r^2 = 0.9976$, $P < 0.001$). Both inward and outward adaptations were accompanied by gradual changes of the PB, which differed qualitatively for the two forms of adaptation. During outward adaptation, both the onset and the peak of the PB gradually moved to later points in time (Fig. 2*B*, based on 13,228 saccades, and 2*E*, based on 17,682 saccades) until, at the end of adaptation, both had been delayed by 24 and 31 ms, respectively, relative to the preadaptation PB. On the other hand, the tight relationship between saccade end and PB end was fully maintained (Fig. S5*B*, burst end = 0.6556 ms + 0.99* saccade end, $r^2 = 0.97$, $P < 0.001$; paired *t* test, saccade end vs. saccade duration, $P > 0.5$).

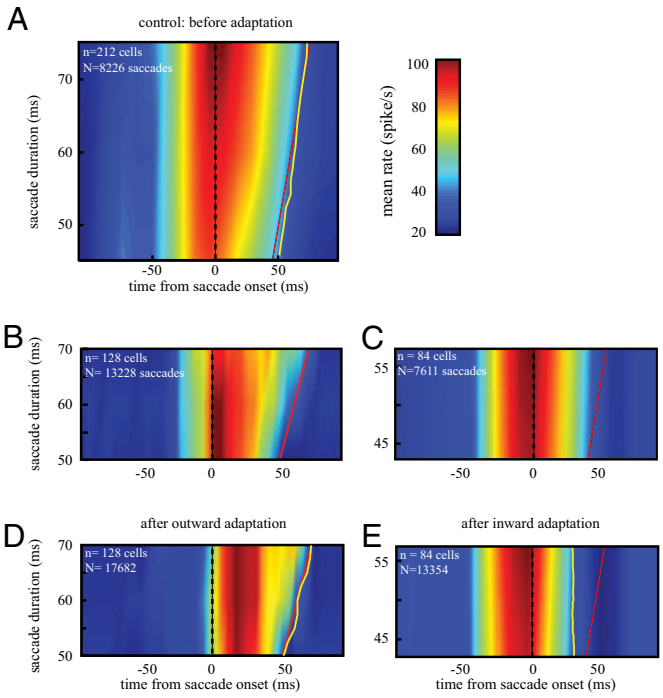


**Fig. 2.** Effect of STSA on PC PB. (*A*) PB before STSA. PB plotted as a function of saccade time (*x* axis; 0, saccade onset) and duration (*y* axis), measured in discrete time steps (*x* axis: 1 ms, *y* axis: 2.5 ms). PBs during outward (*B*) and inward adaptation (*C*) were collected at a level of adaptation, when the gain change achieved lay between 5% and 10%; (*D* and *E*) PBs after stable outward (*D*) and inward adaptation (*E*) (gain change >15%). Black dashed, red, and yellow lines depict, respectively, saccade onset, saccade offset, and PB end.

In contrast, during inward adaptation, the whole PB moved to the left, peaking earlier and ending earlier (Fig. 2*C*, based on 7,611 saccades, and Fig. 2*F*, based on 13,354 saccades). It is particularly noteworthy that the PB not only ended earlier relative to the preadaptation burst but also considerably earlier than the adapted saccade, independently of saccade duration at 30–32 ms after saccade onset. In other words, inward adaptation completely breaks the tight relationship between PB offset and saccade end (Fig. S5*C*, burst end = 34.076 ms + 0.0568* saccade end, $r^2 = 0.4167$, $P = 0.23$; paired *t* test, saccade end vs. saccade duration, $P < 0.001$) that characterizes unadapted saccades as well as increased amplitude saccades resulting from outward adaptation. How can STSA change the PB so smoothly and consistently, although individual PCs change in a seemingly incoherent pattern? An answer is provided by a look at the timing of those PCs that fired saccade-related bursts after adaptation. In the case of inward adaptation, these were the same PC ($n = 67$, $PC_{in}$) that also fired saccade-related bursts before adaptation. However, the group of PCs studied during outward adaptation consisted of two main subgroups; the first comprised PCs that fired saccade-related bursts before as well as at the end of adaptation, $PC_{out\text{-}11}$, ($n = 40$, 31%), whereas the second group ($n = 43$, 34%) consisted of those PCs that were not saccade-related before adaptation but fired saccade-related bursts at the end of adaptation, $PC_{out\text{-}01}$. It must be noted that the reverse was not observed, i.e., no saccade-related PC lost its burst as a consequence of outward adaptation. Fig. 3 *A*, *C*, and *E*, show the distributions of the times of peak discharge rates for the three groups of PCs, separately for inward and for outward adaptation and separately for the periods immediately preceding the beginning (groups $PC_{in}$ and $PC_{out\text{-}11}$ only) and end of adaptation (all groups). PCs studied in the outward adaptation task with bursts before adaptation ($PC_{out\text{-}11}$) shifted their peak significantly (before: 7.37 ± 16.8 ms vs. after: 15.25 ± 15.52 ms, *t* test, $P < 0.05$) by on

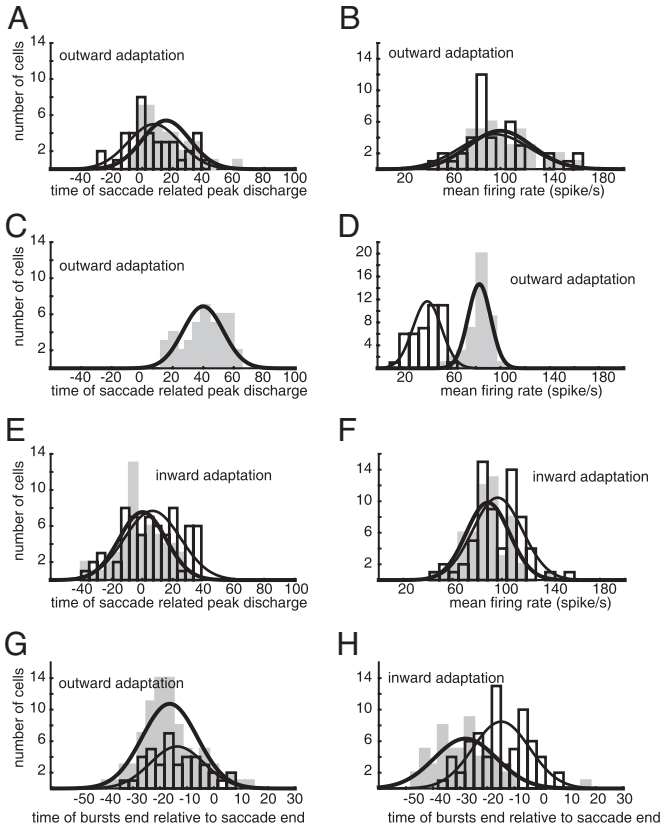


**Fig. 3.** Distributions of times of peak discharge, mean spiking, rates, and times of burst offset for saccades before and at the end of adaptations. (*A* and *B*) Neurons tested for outward adaptation, showing a saccade-related burst before as well as at the end of adaptation ($PC_{out-11}$). Distributions of time of peak discharge rates in milliseconds (*A*) and mean firing rate (*B*) before (white distributions and thin curves) and at the end (gray distributions and thick curves) of outward adaptation. (*C* and *D*) Neurons tested for outward adaptation, which did not exhibit any saccade-related burst before adaptation ($PC_{out-01}$). Format as in *A* and *B*. (*D*) The white distribution and the thin curve plot the background activity of the $PC_{out-01}$ before adaptation. (*E* and *F*) Neurons tested for inward adaptation($PC_{in}$). Format as in *A* and *B*. (*G* and *H*) Distributions of times of burst ends before (white distributions and thin curves) and at the end of adaptation (gray distributions and thick curves). (*G*) All neurons tested for outward adaptation (PCout-01 and PCout-11). (*H*) All neurons tested for inward adaptation.

average 8 ms to later times relative to saccade onset (Fig. 3*A*). Those that had developed new bursts at the end of adaptation ($PC_{out-01}$) fired on average even later, namely 39.41 ± 13.10 ms after saccade onset (Fig. 3*C*), which was significantly ($P < 0.001$) later than the mean of the $PC_{out-11}$ at the end of adaptation. In other words, outward adaptation shifts the population activity to later points in time by delaying preexisting bursts and by generating new, very late bursts. Delaying preexisting bursts was not accompanied by significant changes in discharge rates (Fig. 3*B*). In contrast to outward adaptation, inward adaptation shifted the time of peak discharges to an earlier point (before: 6.41 ± 18.27 ms vs. after: −0.1 ± 15.26 ms, *t* test, $P < 0.03$). This shift was accompanied by a decrease in firing rate (before: 96.16 spikes per s ± 20.08 spikes per s vs. after: 88.25 spikes per s ± 17.53 spikes per s, *t* test, $P < 0.01$). In full correspondence with the behavior exhibited by the population burst for inward adaptation, the burst ends of individual PCs also shifted by, on average, 13 ms to earlier points in time relative to the saccade end (Fig. 3*H*, before: −15.06 ± 10.402 ms; after: −28.2 ± 11.45 ms; *t* test, $P < 0.001$). On the other hand, outward adaptation did not affect the close temporal coincidence of burst end and saccade end that characterizes the unadapted state (Fig. 3*G*, before: −13.825 ± 9.886 ms; after: −16.5783 ± 10.174 ms; *t* test, $P > 0.1$). In sum, the conspicuous adaptation-induced changes characterizing the PB can be led back to distinct changes in the timing of individual saccade-related bursts as well as the birth of new, late bursts in the case of outward adaptation. Hence, the other, less frequent patterns of PC responses observed during adaptation, such as the appearance or disappearance of saccade-related pauses, probably only fine-tune the PB, rather than adding qualitative features, not explicable by the contributions of bursting PCs. Regardless, the distribution of burst ends of individual PCs is far too wide to allow them to determine the timing of saccades. This requires the population signal, which—as discussed next—shows disparate changes that precisely parallel similarly disparate changes in saccade kinematics, resulting from the two forms of adaptation tested.

An analysis of eye movement records collected together with the SS records underlying the PB discussed before shows that outward as well as inward adaptation led to clear deviations of the adapted saccades from the main sequence for unadapted saccades. In the case of outward adaptation, peak saccade velocity stayed constant at the preadaptation level, whereas saccade duration increased in the course of adaptation beyond the duration determined by the preadaptation main sequence (individual example, Fig. 4 *A* and *B*, *Left*; population data, Fig. 4*C*). As the time of peak saccade velocity and, therefore, also the duration of the saccade acceleration phase stayed relatively constant (Fig. S6), adaptation led to an increase in the duration of the deceleration phase and thereby to an increase in the skewness of the saccade (individual example, Fig. 4*A Left*; population data, Fig. 4*C*). On the other hand, in the case of inward adaptation, it was saccade duration that did not change, resulting in a duration of the final, reduced amplitude saccade, which exceeded the duration predicted by the preadaptation main sequence (individual example, Fig. 4*A Right*; population data, Fig. 4*B Right*). The amplitude reduction was the sole consequence of a steady decrease in saccade velocity over the course of adaptation down to 80% of the velocity predicted by the preadaptation main sequence at the end of adaptation (Fig. 4*C*). As the time of peak velocity did not change, the relative shares of acceleration and deceleration also remained unaltered by adaptation and the saccade stayed relatively symmetrical (Fig. S6*B*). During outward STSA, it appears that not only the saccade duration but also the velocity of the movement might be encoded by the PB. This is suggested by Fig. 5*A* (and Fig. S7) and *B*, which illustrate that the deceleration phase of outward-adapted saccades shows a velocity bump that is remarkably close to the bump in the PB.

## Discussion

Unlike the discharge patterns of individual PCs, the collective SS discharge of a larger group of OV PC, the PB exhibits the well directed and continuous changes needed to account for the alterations of saccade kinematics resulting from short-term saccadic adaptation. On the other hand, individual PC-SSs show changes that differ not only quantitatively but even qualitatively between PCs in a manner not reconcilable with the observed changes of behavior. The PB as presented here is first of all a mathematical artifact, based on several dozen PCs preponderantly studied under identical conditions but at different times. Nevertheless, in terms of its size and composition, it is probably a reasonable approximation of the compound signal influencing individual DCN neurons, which receive converging input from a large number of PC axons (15). Our observations on outward adaptation suggest that the major variable controlled by the PB, or in other words, the input to DCN neurons, is the duration of the saccade, determined by the duration of the PB, as suggested earlier (9). However, the subtle changes of the PB profile, paralleling similar changes in the velocity profile of the deceleration part of outward-adapted saccades, may actually indicate that the PB may in fact modify saccade deceleration.

The suggestion that the PB controls the duration of saccades is based on the precise coincidence of PB end and saccade end

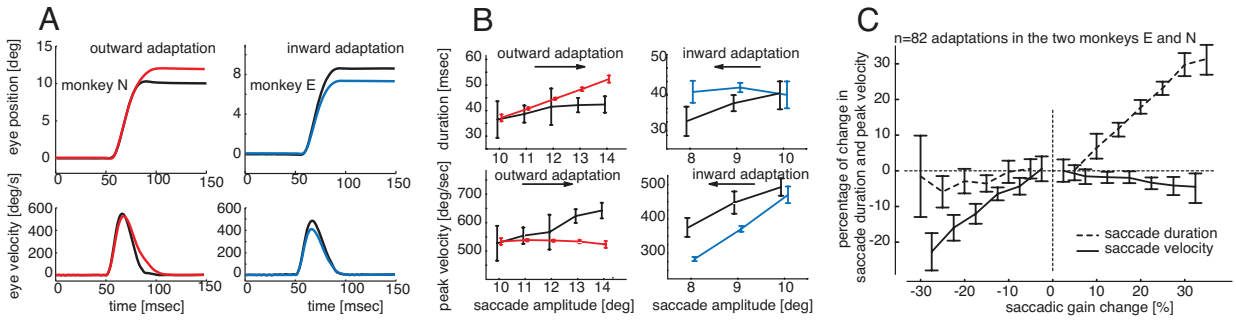


**Fig. 4.** Effect of STSA on saccade kinematics. (*A*) Example of eye position and eye velocity of saccades collected before (black curves) and at the end (colored curves) of adaptation. (*B*) Example of main sequence before vs. during adaptation; saccade duration and peak velocity are plotted as a function of saccade amplitude. The black curves represent the main sequence of saccades collected before adaptation, whereas the colored curves show saccades collected during adaptation (±SEM). *A* and *B* are based on the same dataset. (*C*) Percentage of change in saccade duration and peak of velocity as a function of gain change. Shown are the overall mean ±SEM of all adaptation sessions (82 adaptations in two monkeys) needed to record the 212 neurons considered in the analysis.

that characterizes normal, visually guided saccades and gain-increase saccades resulting from outward adaptation. However, in the case of gain-decrease saccades, induced by inward adaptation, the PB wears off well before the eye movement, an observation that seems at odds with the notion of duration control provided by an OV SS PB.

Actually, this seeming discrepancy could be reconciled with the notion of cerebellar duration control if we assumed that gain-decrease saccades are basically default saccades whose duration is fully determined by the brainstem saccade generator without significant modification by cerebellar influences. To release a saccade whose duration is not extended by the cerebellum, the PC PB should end well before a critical period in which the occurrence of PC input would keep a saccade going beyond the duration set by the brainstem. This might arguably be the reason why the PB preceded the end of the inward-adapted saccades by 10–24 ms, possibly too early to have a major effect on the time course of the ongoing saccade. Actually, it is not only the timing of the PC PB that changes because of inward adaptation but also its strength. In fact, the PC PB for inward adaptation starts to decrease relative to the one for nonadapted saccades 14 ms before saccade onset. In other words, these changes would, in principle, be early enough to have a modulatory influence on the gain-decrease saccade and might underlie the velocity decline that characterizes inward adaptation. In addition to this putative active mechanism, saccade velocity may

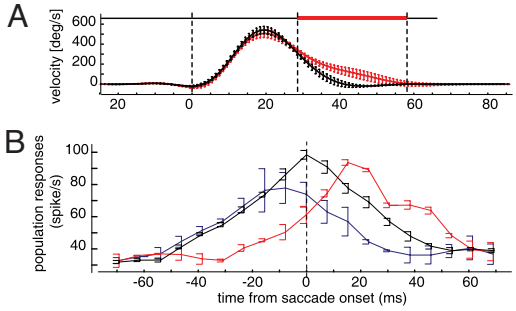


**Fig. 5.** Profile of PC PB. (*A*) Mean velocity (±SE) profile of nonadapted 45 ms saccades (black) when compared with the mean velocity profile of adapted saccades after outward adaptation (red); the red bar above the profiles depicts the period when both profiles are significantly different (running paired *t* test, $P < 0.0005$, corrected for multiple comparison). As a consequence of outward adaptation, mean saccade duration increased from 45 to 58 ms. (*B*) Profile of SS population responses before adaptation of 45-ms-duration saccades (black curve), at the end of inward adaptation (blue curve), saccade duration still 45 ms, and outward adaptation (red curve) (saccade duration increase from 45 to 60 ms) relative to saccade onset. Means (±SE) are depicted.

be influenced by a second, passive mechanism, contributing to the decline in peak velocity, characterizing gain-decrease saccades of monkeys (this study) and those of human subjects (16), a decline in peak velocity that is fully accountable for the amplitude reduction because saccade duration does not change. Similar decreases in peak velocity can be seen when subjects carry out long series of saccades, causing "fatigue," either because of a reduced efficacy of the eye muscles and other components of the oculomotor periphery or because of a loss of attention or motivation (16). In such fatigue experiments, the drop in eye velocity is typically compensated by an increase in duration, keeping saccade amplitude stable. Similar to the loss of outward adaptation, this velocity duration tradeoff preventing fatigue is irreversibly lost after lesions involving the OV region (16). However, even in cases in which outward adaptation is completely lost, at least some inward adaptation may still be observed, arguably reflecting uncompensated fatigue (16, 17). Hence, the lesion observations suggest that the amplitude reduction of inward-adapted saccades has two components, a first, passive component that capitalizes on the reduced velocity resulting from natural fatigue, not affected by the OV lesion, and a second, active one dependent on the PC PB, lost after the lesion. However, there is one observation that is not readily reconcilable with the assumed modulatory influence of the PC PB on saccade velocity, which is contributed by the outward adaptation experiments. Actually, the velocity profiles of outward-adapted and normal saccades are identical except for the added late component responsible for the increase in the duration of outward-adapted saccades. However, the PC PB observed during outward-adapted and normal saccades differ qualitatively in the early phase of the movement, a consequence of the fact that the outward adaptation PC PB is shifted relative to the control PC PB by ≈20 ms.

Recent studies (18, 19) of target neurons of saccade-related PCs in the dorsal fastigial nucleus are in accordance with the notion that a vermal PB sets saccade amplitude by controlling saccade timing. For instance, Scudder and McGee (19) reported that the timing of fastigial saccade-related bursts (FNB) changed during adaptive modification of saccadic gain. When the saccadic gain was adaptively increased, the FNB started later. This last change could easily be interpreted as a consequence of a longer inhibition of the vermal PCs onto their target neurons. In contrast, when the gain decreased, the FNB occurred earlier, suggesting that the "braking" signal sent to the saccade burst generator located in the brainstem stopped the saccade. Similarly, Inaba *et al.* (18) reported that after inward STSA, the FNB started earlier, which indicates that the braking signal sent to the saccade-burst generator located in the brainstem shortened saccade duration.

A PB whose properties appear sufficient to explain the compensatory action of cerebellar cortex on the changing plant can be

understood as the neuronal manifestation of an internal model compensating for changes in plant dynamics. The optimization of this internal model is based on an appropriate modification of the time course and, possibly, also the shape of the PB. This "pruning" of the PB is based on changes of the SS-firing patterns of individual PCs, most probably secondary to changes in the efficacy of their parallel fiber inputs. Such well directed changes in effectiveness could be a consequence of the modulation of the climbing fibers responses. In fact, we have recently shown (20) that STSA leads to a redistribution of CSs with more CSs right around saccade end in the case of inward adaptation and a CS pause around the time of saccade end in the case of outward adaptation. Assuming that CSs induce long-term depression of parallel fiber synapses (21), more CSs around the saccade end should suppress SS activity in this period, thereby shortening the PB as observed. Conversely, in the case of outward adaptation, the absence of CSs around the saccade end should reduce long-term depression and release activity in comparatively late-firing PCs, thereby expanding the PB in time, again as observed.

In conclusion, we suggest that the saccade-related cerebellum guarantees precise saccade amplitudes despite the ever-changing state of the oculomotor periphery by using an optimized PC-SS population signal for the selection of the right saccade duration. The assumption of population coding is first of all an inevitable consequence of the anatomy of the cerebellocortico–nuclear projection, which is characterized by a conspicuous degree of convergence, rendering target neurons unable to listen to individual PCs. The conceptual attractiveness of population coding in this particular system is based on the fact that the anatomical organization of cerebellar cortex in conjunction with well established synaptic learning rules suggest a simple and fast way of optimizing the shape of the population signal (pruning) by emphasizing or deemphasizing the contributions of individual saccade-related inputs to cerebellar cortex according to the needs of the system.

## Experimental Procedures

Two monkeys (*Maccaca mulatta*) were prepared for chronic extracellular single unit and eye position recordings by using search coils as described previously (20). All animal procedures followed the guidelines set by the National Institutes of Health and national law and were approved by the local committee supervising the handling of experimental animals.

**Behavioral Procedures.** The monkeys were asked to focus on a fixation spot located in the center of the monitor for periods of time, which varied randomly between 1,000 and 1,500 ms. At the same time the fixation spot went off, a target appeared randomly in one of eight possible locations in the periphery at 0°, 45°, etc., having a constant distance from the center, varying between 2.5° and 20° in separate blocks. The monkeys were trained to execute prompt and very accurate saccades toward the peripheral target. After determining the preferences of saccade-related PCs (if a PC was isolated) in terms of saccade direction and amplitude, an adaptation series was started by using the standard ''McLaughlin'' paradigm (4) in which the peripheral target changes position in a predefined manner, whereas the saccade is carried out. When a saccade-related PC was isolated, the direction of the adaptation corresponded to the preferred direction of the previously defined cell. When two or more saccade-related PCs were simultaneously isolated, the direction of the adaptation was a compromise between the preferred directions of the individual cells recorded. When the PC did not show any saccade-related activity, the direction of adaptation was randomly chosen. The onset of a saccade was identified by determining the point in time at which eye velocity exceeded 50° per s. The target was displaced either further out (outward adaptation) or back toward the fixation point (inward adaptation). The inward or outward target displacements amounted to 20%, 25%, or 30% of the original target step relative to the fixation point. The direction of adaptation was randomized from one learning session to another. Trials with this intrasaccadic target displacement were repeated several hundred times until a maximal and stable saccadic gain change had been achieved. Gain is defined here as the ratio of saccade amplitude and initial target amplitude. Gain change (%) = [(gain before adaptation − gain during adaptation)/gain before adaptation] *100.

**Electrophysiology.** Postsurgical anatomical magnetic resonance imaging was used to facilitate the localization of lobuli VI and VIIA. The identification of this part of the cerebellum was supported by the characteristic dense saccade-related granule cell background activity and the large number of saccade-related single-units. All recordings were conducted with the monkey in complete darkness. Extracellular action potentials were recorded by using commercial glass-coated tungsten microelectrodes (Alpha Omega Engineering; impedance $<1.2$ megaohms) by using a four-probe multielectrode system (electrode positioning system and multichannel processor, Alpha Omega Engineering). PCs were identified by the presence of spontaneous complex spike discharge. SS of well isolated PCs were discriminated online by using a Multi Spikes Detector (Alpha Omega Engineering). Each PC was observed during a preadaptation baseline session and during saccadic adaptation. Only PCs recorded long enough for seeing a stable gain change of at least 15% were considered in the analysis.

**Data Analysis.** Saccade onset and offset were detected based on a velocity threshold (saccade onset: when velocity reached 20° per s during acceleration phase; saccade offset: when velocity became $<20°$ per s during deceleration phase). The characteristics (time of peak discharge, mean firing rate, and burst offset) of individual saccade-related PC bursts were determined in single trials by applying a Poisson spike train analysis. To exclude spurious bursts, we used the following qualifications: burst onset had to follow the onset of the peripheral target and the burst onset had to be within a period starting 150 ms before saccade onset and lasting maximally until 100 ms after the end of the saccade. A PC was considered saccade-related if saccade-related bursts were detected in at least 50% of the trials. We applied these analyses to compare the 50 preadaptation trials with the last 100 adaptation trials. For the $PC_{out\text{-}01}$, baseline firing rate corresponds to the mean firing rate during the saccade. The distributions presented in Fig. 3 were shown to be Gaussian by applying Kolmogorov-Smirnov tests ($P > 0.05$).

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